I-A

THE DIAGNOSIS AND TREATMENT OF ACIDOSIS

BY

L. G. ROWNTREE, M.D., Sc.D.

MINNEAPOLIS

From the
Transactions of the Association of American Physicians
1916

Reprinted from the Transactions of the Association of American Physicians, 1916

THE DIAGNOSIS AND TREATMENT OF ACIDOSIS

By L. G. ROWNTREE, M.D., Sc.D.
MINNEAPOLIS

Theoretically and practically acidosis is of extreme interest: to the scientist, on account of the ingenious protective mechanism provided by nature for the maintenance of a constant acid base equilibrium; to the clinician, because of its frequency in many clinical conditions. Recently, new methods have been evolved which make possible early and more precise diagnosis, and furnish an insight into the mechanism whereby the acidosis develops. More ready clinical recognition of any condition leads to earlier and usually to more successful treatment, while information relative to the mode of production leads to successful prophylaxis and to rational therapy. These are desiderata of the greatest importance owing to the grave prognostic significance attaching to the development of severe acidosis, the suddenness of its appearance at times, and, above all, to the fact that proper therapy in some instances may tide a patient over a critical period.

The problems of acidosis are embraced in the larger problem of the maintenance of a constant acid base equilibrium in the body. The factors here concerned must be borne in mind since different mechanisms are unquestionably playing a role in the development of the various types of acidosis. That different types do exist is early evident to the student of the subject.

Though much has been written, little of fundamental importance has been added to our knowledge of the maintenance of this equilibrium since the masterly presentation of the subject by L. J. Henderson, in 1909.[1] Clinically, great strides have been made in

our knowledge of acidosis from the stand-points of methods and diagnosis and in our knowledge of its clinical associations.

One fact must be borne in mind. Idiopathic or primary acidosis is unknown. Acidosis is always secondary. It arises in the course of many pathological processes which in turn are influenced by its presence. It becomes a part of different vicious cycles. Its investigation is rendered more difficult by its manifold clinical associations. Variations in types which can be observed clinically or elicited through laboratory studies may frequently be dependent upon associated diseases.

Factors Maintaining Acid-base Equilibrium. Four great factors at least are concerned in maintaining acid-base equilibrium. These are (1) the excretion of CO_2 by the lungs; (2) the activity of the kidney whereby an acid urine is separated from blood which is alkaline; (3) the peculiar property of the blood—the so-called buffer action to acid and alkali; (4) finally, the formation of ammonia which aids in the neutralization of acid when the fixed bases are no longer available. Changes in regard to factors (1), (2), and (3) are almost invariably encountered when large quantities of acids are produced within the body or introduced from without. Increased ammonia production, however, is not a constant accompaniment of clinical or experimental acidosis. Certain features of each factor are worthy of special consideration.

1. *Respiration.* CO_2 is constantly transferred from seats of high to seats of low tension, *i. e.*, from the tissues, where the CO_2 is formed and where the tension is high, to the blood, to the alveolar air, and finally to the external air where its tension is lowest. In this process the $NaHCO_3$ of the plasma plays an extremely important role since stronger acids replace CO_2, which in turn is readily excreted, leaving a neutral salt. Henderson refers to the bicarbonate as the first line of defences. They protect the body from acids in the following way: $NaHCO_3 + HCl = NaCl + H_2O + CO_2$.

The equivalent of several hundred cubic centimeters of a normal acid is eliminated by the lungs in twenty-four hours.

2. *Excretion of Acid in Urine.* The kidneys excrete an acid urine while the blood supplying them is alkaline. In this way the body is freed of acid and acid phosphates while bases are saved to

the organism. Some alkali is excreted with the phosphate, but a new function of the kidney is now recognized, *i. e.*, conservation of bases.

Thus: $Na_2HPO_4 + HCl = NaCl + NaH_2PO_4$, the disodium phosphate serving to take care of both the acids. On the other hand the following reaction may occur, under which conditions the alkali or bicarbonate reserve of the blood is increased while acid is being excreted, $Na_2HPO_4 + H_2O + CO_2 = NaH_2PO_4 + NaHCO_3$. That this function of the kidney is one of great importance is shown by the fact that the alkali so saved approximates 200 to 800 c.c. $\frac{N}{10}$ NaOH per diem.

3. *The Buffer Action of Blood.* By the "buffer action" of a mixture is meant its ability to take up considerable amounts of acid or alkali when these are added to it without appreciable changes in hydrogen ion concentration. The blood is such a buffer mixture, owing largely to its content of carbonates, phosphates and, to a lesser extent, its protein.

Last year, in presenting the dialysis-indicator method before the Association of American Physicians, it was stated that it was being employed in a study of the buffer value of the blood. A report by Van Slyke, Stillman, and Cullen appeared in April, 1915, demonstrating the decrease in reserve alkalinity in acidosis. Our paper[2] appeared in the *Archives of Internal Medicine* for April, 1916.

Mode of Expression of Results. All results are expressed in terms of c.c. of $\frac{N}{50}$ HCl or NaOH per 2 c.c. of blood.

The final results appear in Table I, from which it is evident that the alkaline reserve of the blood is decreased, and in addition, what has not been recognized clinically, that the acid reserve or buffer against alkali is also decreased.* The total buffer value is therefore diminished.

4. Utilization of NH_3 after the fixed alkalies have failed occurs in acidosis associated with marked ketonuria. As already indicated, this mechanism, however, is not called into play at all in certain types of acidosis.

* The decrease is not constant since some instances of normal buffer in both clinical and experimental acidosis have been encountered in our study.

TABLE I.—SUMMARY OF ACID, ALKALI, AND TOTAL BUFFER VALUES FOR THE VARIOUS CASE GROUPS EXPRESSED AS GROUP AVERAGES

		No. of cases and determinations.	Acid.	Alkali.	Total.
Normal individuals . .		24	0.18	0.18	0.36
9	True . . .	9	0.075	0.056	0.13
Acidosis		16			
24	Compensated	6	0.1	0.1	0.2
		8			

LABORATORY STUDIES OF ACIDOSIS.* VALUE AND LIMITATION OF METHODS. In this connection there are three general lines of approach: studies of the urine, the expired air, and the blood. These all reflect tissue changes. As nothing is known at present concerning tissue acidosis the pH of the blood is generally accepted as the index to acid base equilibrium of the organism as a whole. Unquestionably the blood studies constitute the most direct approach, although studies by indirect methods furnish extremely reliable and valuable data.

1. *Urinary Studies.* In the study of the urine the ammonia content, the quantity of acid bodies, the hydrogen ion concentration, and the reaction before and after the "alkali tolerance test"[3] are usually determined. In reality, information concerning renal function is also essential. In renal insufficiency the "alkali tolerance test" as now employed in the study of acidosis is not only useless, but is misleading. It is obviously impossible to base conclusions relative to the impoverishment of the tissues in alkalies on the failure of urine to become alkaline following the administration of cabonates or bicarbonates in amounts ordinarily sufficient to render it alkaline. The kidney simultaneously fails to excrete all other substances in normal fashion, with the possible exception of water. The findings cannot be interpreted, therefore, as indicating acidosis unless the excretory capacity of the kidney is known to be normal. This statement must not be interpreted as meaning that the test is not of value, but it does mean that the test is only applicable in selected cases.

* The writer wishes to acknowledge his indebtedness to Miss Winifred Swift for much technical assistance.

The ammonia of the urine may be increased or decreased, depending upon the type of acidosis. In diabetes and eclampsia, for example, it is of distinct importance, whereas in certain types of nephritis, as indicated by the studies of Palmer and Henderson, it has no great significance.

Acetone bodies (acetone, diacetic) appear in the urine under a large variety of conditions, but do not reflect the true state of the neutrality regulating mechanism. They are not constantly found in acidosis nor is their presence always indicative of its existence. Acidosis can exist without ketonuria. These terms are not synonymous, though often considered so.

The hydrogen ion concentration of the urine in health and disease has been carefully investigated by Palmer and Henderson.[4] The normal variations are so great that the findings have but slight clinical significance.

At best, studies of the urine yield information relating solely to the amount of acid excreted in the urine and not to the amount present in the blood and tissues. By inference they admit of certain deductions under definite considerations.

2. *Studies of Respiration.* The determination of the CO_2 of the alveolar air is an indirect but very valuable method of study in acidosis, the findings probably indicating approximately the bicarbonate reserve of the blood. Alveolar air may be collected by any one of several methods:* (*a*) Haldane,[5] (*b*) Plesch,[6] and (*c*) Fridericia.[7] The first and last necessitate intelligent coöperation on the part of the patient, whereas the Plesch method is generally applicable. Dr. R. L. Levy, who collaborated with me in Baltimore in these acidosis investigations, has perfected a mask which is fashioned somewhat after the one earlier employed by Dr. John King, of Baltimore. It utilizes the principle of rebreathing as described by Plesch. It has been used with the Haldane method in the CO_2 determinations here recorded.

Air collected by the Plesch-Levy method can also be determined in the Fridericia apparatus. The result of a series of such determinations is compared with those of the Haldane method in Table II.

* The details concerning this will appear in a separate publication.

TABLE II.—COMPARISON OF FRIDERICIA AND HALDANE METHODS OF DETERMINING ALVEOLAR CO_2 WITH PLESCH-LEVY COLLECTION

Case.	Hosp. No.	Temp.	Fridericia, mm. Hg.	Haldane, mm. Hg.	Remarks.
F. . . .	8477	22	29.8	29.6	Pregnancy at term.
C. . . .	8455	22	22.3	21.9	9 days postpartum.
P. . . .	8368	22	31.3	30.7	9 " "
L. . . .	8487	22	23.2	22.9	7 " "
S. . . .	8498	22	40.6	40.4	12 " "
B. . . .	8508	22	35.2	34.8	9 " "
H. . . .	8522	22	35.3	35.06	10 " "
C. . . .	..	23	47.9	47.4	Normal.
Z. . . .	..	23	44.3	44.0	Normal.
G. . . .	..	23	49.2	48.9	Normal.

Peabody's[8] demonstration of increased sensitiveness of the respiratory center through rebreathing various percentages of CO_2 is an important addition to our knowledge of acidosis. But the effects of other factors, especially drugs (morphin) and various diseases upon the center, may modify or overshadow this influence.

3. *The Blood.* This is the logical and direct avenue of approach. Technical difficulties, however, lead to the introduction and use of the numerous indirect methods already described. Recent work has resulted in new methods which make the direct investigation possible clinically. The methods in use for studying the blood determine:

1. Hydrogen ion concentration.
   (*a*) Hydrogen electrode method.[9]
   (*b*) Dialysis-indicator method.[10]
2. The buffer value of blood—herein described.[11]
3. The alkaline reserve (Van Slyke).[12]
4. Titratable alkalinity (Sellards).[13]
5. The curve of hemoglobin dissociation (Barcroft).[14]
6. The quantity of acetone bodies (Schaffer and Marriott).[15]

The fact that the gas-chain method of determining the pH of the blood requires a delicate and expensive piece of physicochemical apparatus as well as considerable technical training has militated against its use in clinical medicine. Recently the dialysis-indicator method has been introduced. In collaboration with Dr. J. F. McClendon[16] I have had the opportunity of comparing its findings with those of the electrometric method (Fig. 1) as devised and used by him. Samples of blood from various sources have been taken, inde-

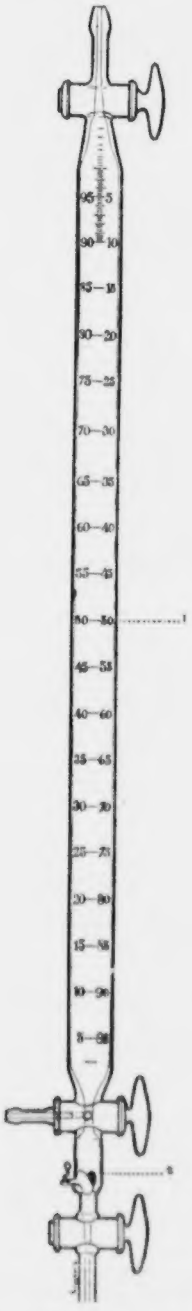


FIG. 1.—McClendon's combined tonometer and hydrogen electrode. 1. Mixing chamber. 2. Electrode. To appear shortly in Jour. of Biol. Chem.

pendent readings being made on them by the two methods. The results of this study appear in Table III.

TABLE III.—pH AS DETERMINED BY THE ELECTROMETRIC AND THE DIALYSIS-INDICATOR METHODS. DETERMINATIONS WITH ACCURATE CONTROL OF CO_2 TENSION*

No.	Material, 1.5 c.c.	CO_2 tension, per cent.	pH. Electrometric.	pH. Dialysis-indicator
1	Plasma	1	8.05	8.1
2	"	3	7.9	7.9
3	"	5	7.6	7.6
4	"	10	7.43	7.4
5	"	10	7.4	7.4

EXPERIMENTAL DATA

Dog.	Weight, kg.	Condition.	pH. Electrometric.	pH. Dialysis-indicator.
Ia	11.1	Normal	7.5	7.5
b	..	150 c.c. $\frac{N}{2}$HCl	6.8	6.8
c	..	180 c.c. 8% $NaHCO_3$	7.5	7.5
d	..	465 c.c. 8% $NaHCO_3$	7.7†	7.65‡
II	11.8	In shock	7.2	7.15
IIIa	17.1	Normal	7.4	7.4
b	..	In shock	7.2	7.15

CLINICAL DATA

Patient.	Hospital No.	pH. Electrometric.	pH. Dialysis-indicator.
T.	8140	7.5	7.45
E.	8234	7.5	7.5
S.	8236	7.6	7.6

(See Fig. 1.)

More satisfactory agreement§ could not be desired. The rapidity and ease with which absolute values are obtained by the new method warrants its wide use in studies‖ of either acidosis or alkalosis.

* McClendon's combined tonometer and hydrogen electrode.

† Electrometric method on arterial blood.

‡ Dialysis-indicator method on venous blood.

§ More intimate acquaintance with the dialysis-indicator method demonstrates that great precautions are necessary in order to minimize the loss of CO_2. Blood is therefore drawn directly into a specially devised tube provided at each end with rubber connection and pinch cocks. Distally is attached, by the rubber connection, a second tube which is also partially filled before the clamps are applied. Blood is therefore drawn without exposure and without loss of CO_2. The desired amount of blood is allowed to flow into the dialyzing sac, which is lowered into the salt solution. The upper part of the sac is cut off and the tube stoppered during dialysis. Prolonged constricting by a tourniquet must be avoided in the collection of blood.

‖ Dialysis also offers an excellent opportunity for the study of abnormal acids present in the blood in acidosis. In the recent vividiffusion experiments of Abel, Rowntree and Turner,[17] lactic acid, β-oxybutyric acid, alanin, valin and histidin were isolated. A study of the dialysate from the blood in acidosis would unquestionably prove profitable.

Since a change in the pH only obtains after the protective mechanism has failed, peculiar significance attaches to its presence. Obviously compensated grades of acidosis will not be detected unless resort is had to one of the other tests.

The buffer value of blood has already been discussed. Scientifically these studies throw an interesting side light on the mechanism involved in the production of acidosis, but inasmuch as the total buffer value is not always decreased in acidosis and as the method as described requires considerable time and labor it will probably not come into wide use clinically.

The alkaline reserve or bicarbonate content of the blood as determined by Van Slyke yields information of the greatest significance clinically and scientifically. The method is readily applied, yields reliable and valuable data, and will unquestionably play a very important role in all future studies of the subject.

Sellard's test of titratable alkalinity yields valuable empirical data. It is to be commended for its simplicity. It is a gross index of acidosis and can be used by those lacking the time and equipment for the more refined methods.

With the curve of the *hemoglobin dissociation* my acquaintance has been too casual to justify an expression of opinion. Technical difficulties preclude its wide use in a clinical procedure.

The quantitative method of determining the acetone bodies in the blood is unquestionably of great importance, particularly in diabetes, but it is technically removed from general use.

Essentials in Determining Acidosis. The number of methods has increased to such an extent that it is essential to determine which can be discarded without loss and also what test or combination of tests yields all the desirable information in a given case. This necessitates an intimate familiarity with the applicability, limitations and significance of each test.

In my opinion the most essential factors to determine are the reserve alkalinity, the alveolar CO_2, and the pH of the blood. The best methods* are: for the first, the Van Slyke method; for the second, the Plesch-Levy collection, with gas analysis by the Haldane

* Marriott has recently introduced colorimetric methods for the determination of alveolar CO_2 and alkaline reserve which may prove to be extremely valuable.

apparatus; and for the pH, the dialysis-indicator method. These yield quantitative data and indicate whether acidosis exists, whether it is compensated or absolute. Depending upon the underlying disease and the type of acidosis, other tests are desirable at times.

ACIDOSIS AND NOMENCLATURE. If I desired to precipitate a discussion I would merely ask the question, What is acidosis? The term itself is a misnomer, since a pH greater* than 7.0 is rarely or never encountered clinically. Acidosis is a loosely used term. This Association would do a real service were it to appoint a committee to consider the question of nomenclature.

Inasmuch as this paper discusses acidosis, it becomes necessary to declare my attitude in this connection. Our custom has been to call all cases with a pH of the blood greater† than 7.4, *true acidosis;* all cases showing a normal pH but a decrease in alveolar tension and in the alkaline reserve of the blood, *compensated acidosis.* That this is far from ideal is admitted since "acidosis," though universally sanctioned, is a misnomer and since compensated acidosis is used to express an acidosis that is not an acidosis since a change in the pH of the blood has been prevented. Hasselbach[19] has also made this distinction.

CLINICAL EVIDENCE OF ACIDOSIS. CLINICAL ASSOCIATIONS. In acidosis respiratory changes are usually present. Hyperpnea (air hunger) is extremely common, but not absolutely constant. It always suggests acidosis and demands investigation. It does not invariably indicate acidosis for unmistakable hyperpnea has been encountered at times in animals, the subjects of experimental alkalosis, *i. e.*, in animals receiving large quantities of $NaHCO_3$ intravenously. The so-called acetone odor of the breath is most frequently encountered in cases showing ketonuria.

Acidosis is found in association with the following diseases and conditions:

1. Diabetes.
2. Renal, cardiorenal and cardiac disease.
3. Cachectic states and severe anemias.
4. Severe diarrhea (particularly in children).

* By "Greater pH" is meant a greater "H" ion concentration, *e. g.*, pH 7.3 indicates H ion concentration greater than pH 7.4

† Levy

5. Cholera. Sellards.[21]

6. Starvation.

7. Pregnancy[22] and eclampsia.

8. Postoperative or postanesthetic conditions, particularly in surgical shock.

9. Certain febrile diseases.

During the course of the last two years, out of several hundred patients on whom some of these studies have been made, between 30 and 35 cases of true acidosis have been found. A few of the more interesting results will be considered.

Acidosis in Diabetes. I. G. V. H., Med. No. 33876, Johns Hopkins, showed marked air hunger, urinary ammonia of 3 gm., and pH 7.25. After receiving 500 c.c. of 4 per cent. $NaHCO_3$ the pH was 7.45, this persisting for twenty hours. The acetone bodies, determined as acetone by Dr. Marriott, were 240 mgm. to 100 gm. of blood. The patient died in typical coma, the blood serum before death reading 7.65, *i. e.*, normal.

This indicates that death was not due to increased hydrogen ion concentration of the blood and is in keeping with the findings of Ehrmann and Esser[23] who demonstrated that the sodium salts of oxybutyric acid are capable of producing symptoms analogous to those found in diabetic coma.

The importance of this finding cannot be too strongly emphasized, since it indicates that alkali is of value in diabetic acidosis only in so far as it corrects the acidosis. I have seen at least three diabetics die after alkali therapy which resulted in the return of pH of the blood to normal. The condition of tissues, however, remains unknown. Alkali therapy should be used with a specific object in view and the amount should be controlled by laboratory studies. I have seen patients receive $NaHCO_3$ in amounts closely approximating in grams per kilogram the lethal dosage for dogs.

Acidosis in Renal and Cardiorenal and Cardiac Disease. At times acidosis plays a definite role in renal, cardiorenal and cardiac diseases. It may or may not develop in marked renal insufficiency. The findings in a fatal case of chronic interstitial nephritis (small granular kidney) seen in consultation with Dr. J. P. Schneider of Minneapolis emphasize the importance of such studies. The results appear in Table IV.

TABLE IV.—UREMIA AND ACIDOSIS. R.—SWEDISH HOSPITAL

Date.	Alveolar CO_2, mm. Hg.	pH, blood.	CO_2 cap. of plasma, c.c. of CO_2	Urea N., mgm.	Non-p. N. per 100 c.c.	Creatinine, ll	Phthalein and Ambard's constant	Remarks
April 17	29.72	7.2	..	97.0	171	..	Ph. 7 per cent.	$NaHCO_3$ 15 gm. daily.
April 19	26.15	7.3	30.4	181.0	206	24	Ph. trace Am. con. 1.02	600 c.c. 4 per cent. $NaHCO_3$ I. V
April 20	25.67	7.5	37.57	158.0	203	19	Am. con. 1.09	
Before April 22	..	..	24.59	91.0	171	..	..	600 c.c. 4 per cent
After	..	7.6	26.45	..	..	..	..	$NaHCO_3$ I. V
April 24	30.4	7.45	..	87.0	162	..	Am. con. 0.41	
Before April 25	..	7.3	31.7	84.5	..	..	..	Transfusion
After	39.4	7.45	31.94	67.0				

In the acidosis accompanying renal insufficiency the CO_2 of the alveolar air may be tremendously decreased, in one instance reaching as low as 7 mm. Hg., and in 4 of our cases lower than 12 mm. Hg. The acetone bodies did not accumulate in the blood nor was there increase in the urinary ammonia in 2 of these cases in which these features were determined. Temporary benefit, in the clearing up of coma, in the relief of dyspnea, and in urinary secretion, together with increase in reserve alkalinity of the blood and correction of the pH, are observed at times following the administration of alkali. But I have yet to see anything approaching permanent results under these conditions except in one instance of renal insufficiency and acidosis accompanying an acute exacerbation in a case of chronic nephritis.

The role of acidosis in the production of dyspnea in patients with uncomplicated valvular disease and acute decompensation[24] is slight. The dyspnea exists with and without acidosis but the acidosis is more marked and appears only during the very acute stage, rapidly disappearing with clinical evidence of improvement. But in cardio-renal disease, as might be expected, it becomes a more important factor.

Acidosis in Cachexia and Anemia. In cachexia and anemia acidosis is occasionally encountered.

S., a case of carcinoma of the stomach, with marked metastases in the liver, died in profound coma with acidosis showing a pH of 7.35, a positive Sellard's test, an alveolar CO_2 of 11.4 Hg., and a decreased reserve alkalinity. Typical air hunger was present. In experimentally induced anemia in a dog acidosis did not develop after reducing the Hb. to 45 per cent. by repeated bleedings. (See Table V.)

Table V.—Effects of Bleeding

Dog.	Time.	Weight in kgm.	Alveolar CO_2 in mm. Hg.	Alkaline reserve in mm. Hg
I.	June 14, 1916:			
	Before bleeding	17.0	39.83	29.13
	Immediately after bleeding 500 c.c.	..	39.83	30.0
	June 16, 1916	16.3	38.83	46.51
II.	June 14, 1916			
	Before bleeding	21.8	40.57	37.38
	Immediately after bleeding 600 c.c.		40.5	37.38
	June 16, 1916	21.5	41.03	44.67

Acidosis in Pregnancy and Eclampsia. It has been claimed that acidosis occurs in pregnancy.[25] True acidosis does not occur, and compensated acidosis, when present, is negligible.

The association of acidosis with eclampsia is interesting. Our series is too small to admit of any conclusions relative to its constancy; 8 cases only have been studied; true acidosis was present in 5. The findings appear in Table VI.

Table VI.—Acidosis in Eclampsia

Name.	Date.	pH.	Alveolar CO_2	Carbon dioxid blood	Remarks.
K.	..	7.3	..	..	Recovery.
H.	June 9, 1915	7.3	..	..	T.n.P.N., 307 mgm.; urea N., 256 mgm.; [illegible] tolerance 15 gm.
B.	April 28, 1916	7.35	30.38	24.67	Died.
H.	April 29, 1916	7.35	23.02	25.3	Recovery.
P.	May 2, 1916	7.45	..	33.22	Puerperal convulsions.
S.	June 3, 1916	..	35.0	34.9	Died.
L.	June 22, 1916	7.35	35.0	33.0	Convulsions.
H.	June 27, 1916	7.5	35.3	39.0	

Blood from the cord of the baby in Case II was secured and the pH of the serum determined as 7.3. Both patients recovered in spite of the acidosis.

These findings in eclampsia carry therapeutic significance, and indicate that alkali therapy should be tried.

Acidosis in Anesthesia and Surgical Shock. Four post-operative cases exhibiting clinical evidences of acidosis were studied: 2 prostatectomies, 1 nephrotomy, and 1 drainage of gall-bladder, with bile peritonitis. All showed true acidosis.

Clinically we have had no opportunity for the study of acidosis in relation to surgical shock. In collaboration with Dr. J. F. Corbett,* experimental shock is being studied at present. Here true acidosis develops, as indicated in Table VII.

Table VII.—Shock Experiments

Dog.	Time.	Weight, kg.	pH.	Alkaline reserve.	Alveolar CO_2.	Remarks
AE 916	9.30	25.0	7.4	43.7		
	1.30	..	7.1	38.6	27.6	
	1.30	..	7.0	28.4	32.8	
AE 913	8.30	21.8	7.4	54.6	40.9	
	1.30	..	7.0	32.1	37.1	
AE 926	9.30	25.0	7.45	51.7	43.9	
	12.30	..	7.3	..	22.6	
	3.30	..	7.1	32.1	25.6	
AE 911	9.30	18.6	7.5	51.6	48.3	
	12.30	..	7.45	38.5		
	1.30	..	7.2	..	39.5	
AE 949	8.40	19.1	7.5	56.2	54.7	3.25, 150 c.c. Ringer's solution.
	3.30	..	7.3	42.9	26.4	
	4.00	..	7.1	38.0	41.4	3.30, 100 c.c. 5 per cent. $NaHCO_3$.
	5.30	..	7.4	42.0		
30	8.30	24.0	7.45	52.9	56.5	3.03, 200 c.c. Hogan's solution.
	3.03	..	7.35	28.9	26.8	
	3.22	..	..	39.3	40.8	3.22, 200 c.c. Hogan's hemolized.
	4.05	..	..	46.5	47.9	

The effect of $NaHCO_3$ upon blood-pressure in shock affords additional evidence of the existence of acidosis. Tracing I is a chemographic tracing showing the fall of blood-pressure accompanying shock and the response to the administration of $NaHCO_3$. The effect of Ringer's solution is also indicated. Tracing II demon-

* Separate report will appear later.

TRACING I

DOG NO. 949. WT. 42 LBS.

Normal tracing at 8.40 A.M. Five per cent. bicarbonate used.	Trauma, 8.55 to 9.30, 10.35 A.M.	Trauma, 15 min. at 15 min. intervals, 2.00 P.M.	After Ringer's solution, 150 c.c., 3.25 P.M.	After bicarbonate solution, 100 c.c., 3.34 P.M.	3.50 P.M.

TRACING II

DOG NO. 30. WT. 54 LBS.

Normal tracing at 9.30 A.M.	Trauma, 11.55 A.M. to 12.20, 1.00 P.M.	Trauma, 2.45 to 3.00, 3.05 P.M.	After Hogan's solution, 80 c.c., 3.11 P.M.	After Hogan's solution, 120 c.c., 3.17 P.M.	After Hogan's solution, 200 c.c., 3.51 and 3.57 P.M.	Death, 4.34 P.M.

strates the effect of Hogan's gelatin alkaline mixture in experimental shock.

ACIDOSIS IN STARVATION. It is a common belief that starvation results in acidosis. That acidosis may occur is not denied, but as the result of study of starvation dogs we feel convinced that the role of acidosis is extremely slight. Here, again, ketonuria is the more marked feature. From an uncompleted study now in progress in my department by Dr. Northington and Dr. Grave* it appears that the role of acidosis is almost negligible for ten days at least in starvation. Ketonuria usually develops within forty-eight hours and its presence has been construed into evidence for acidosis. Alkaline reserve, alveolar CO_2, and pH of the blood remain normal for the first ten days but later the alveolar CO_2 indicates a slight tendency to decreased tension.

TREATMENT OF ACIDOSIS. Alkali treatment is always indicated in acidosis, because a diminution in bicarbonate reserve as pointed out, by L. J. Henderson, is an invariable accompaniment of acidosis regardless of other coexisting changes. The degree of the acidosis should be determined preliminary to the administration of alkali, since the degree of acidosis controls the intensity of treatment. The more severe the acidosis the more alkali is indicated. Alkali should be administered at least until the pH of the blood returns to normal. It is desirable, perhaps, to correct the alveolar CO_2 and alkali reserve as well, although this is not always so readily accomplished.

When the treatment is intensive, alkalosis results, a condition but little studied and little understood. Chart I† illustrates the gradual development of acidosis and of alkalosis as the result respectively of slow administration intravenously of $\frac{N}{2}$ HCl of 5 per cent. $NaHCO_3$. Death resulted in both instances.

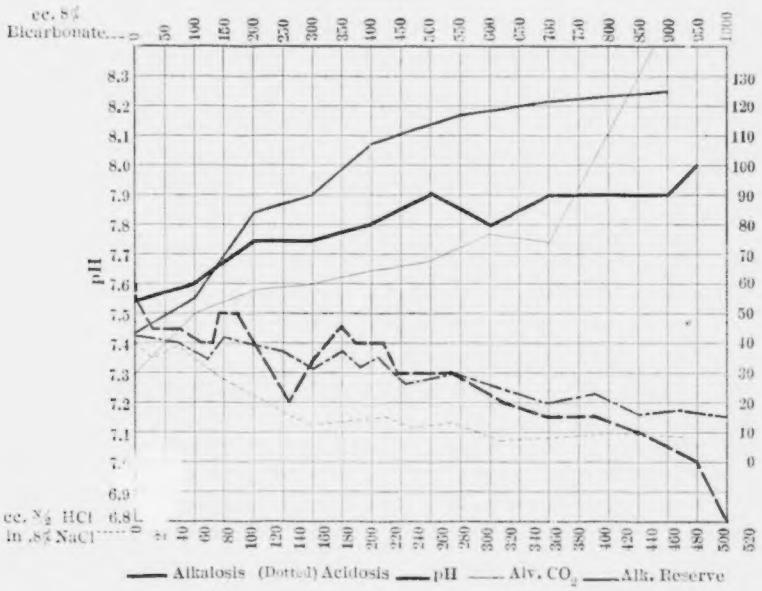
The usual clinical effects of alkaline treatment are relief of dyspnea, diuresis, with occasionally mental improvement. With lethal amounts of alkali coarse tremors and rigidity develop, and finally vomiting, convulsions, and relaxation of the sphincters. Rigor mortis is immediate and extreme.

* To be published later.

† In alkalosis the CO_2 of blood and of the alveolar air are widely divergent.

Clinically, at times, edema and ascites develop during alkali administration. Aside from alkali therapy alkalosis is rarely encountered. Levy and I have found it only in the following conditions: typhoid following transfusion in primary and secondary anemia, and in nephritis. Wilson and Stearns[26] demonstrated its presence in experimentally induced tetany in dogs.

CHART 1



At the present time it must be admitted that our knowledge of acidosis is not profound. Relatively simple methods of determining its existence and intensity are now available, the same methods serving for the control of therapy. Through their use a deeper understanding of acidosis must result. More exact, and therefore more effective, treatment can be confidently anticipated.

BIBLIOGRAPHY

1. Henderson, L. J. Das Gleichgewicht zwischen Basen und Säuren im tierschen Organisms, Ergb. d. Physiol., 1909, viii, 254.

2. Levy and Rowntree. A Study of the Buffer Value of the Blood. Arch. Int. Med., April, 1916, xvii, 525.

3. Sellards, A. W. The Determination of the Equilibrium in the Human Body between Acids and Bases, with Special Reference to Acidosis and Nephropathies, Johns Hopkins Hosp. Bull., 1912, xxiii, 289.

Sellards, A. W., A Clinical Method for Studying Titratable Alkalinity of the Blood and its Application to Acidosis, ibid., 1914, xxv, 101.

Palmer and Henderson. Clinical Studies on Acid-base Equilibrium and the Nature of Acidosis, Arch. of Int. Med., 1913, xii, 153.

4. Palmer and Henderson. On the Extremes of Variation of the Concentration of Ionized Hydrogen in Human Urine, Jour. Biol. Chem., 1913, xiv, 81.

Henderson and Palmer. On the Retention of Alkali in Nephritis, ibid., 1915, xxi, 57.

5. Haldane and Priestley. Jour. Physiol., 1905, xxxii, 225.

Haldane and Poulton. Ibid., 1908, xxxvii, 390.

Haldane and Boycott. Ibid., 1908, xxxvii, 355.

Haldane and Douglas. Ibid., 1909, xxxviii, 420.

6. Plesch. Method of Obtaining Alveolar Air, Ztschr. f. exp. Path. u. Therap., 1909, vi, 380.

7. Fridericia. Eine klinische Methods zur Bestimmung der Kohlensäurespannung in der Lungenluft, Berlin. klin. Wchnschr., 1914, li (2), 1268.

8. Peabody. Clinical Studies on Respiration, No. 1. The Effect of CO_2 in the Inspired Air on Patients with Cardiac Disease, Arch. of Int. Med., November 15, 1915, p. 846.

9. Botazzi. Der Harn sowie die ubrigen Ausscheidungen und Korperflussigkeiten, edited by C. Neuberg, Berlin, 1911.

Hasselbalch and Lundsgaard. Biochem. Ztschr., 1912, xxxviii, 77. Lundegaard. Ibid., 1912, xli, 247.

Peters. Physiol. Soc. Prac., January, 1914.

Peabody. Studies on Acidosis and Dyspnea in Renal and Cardiac Disease, Arch. Int. Med., 1914, xiv, 236.

Milroy. Quart. Jour. Exper. Physiol., 1914, viii, 141.

Lundegaard. Biochem. Ztschr., 1912, xli, 247.

10. Levy, Rowntree, and Marriott. A Simple Method for Determining Variations in the Hydrogen-Ion Concentration of the Blood, Arch. Int. Med., September, 1915, xvi, 389.

11. Levy and Rowntree. A Study of the Buffer Value of the Blood. Arch. Int. Med., April, 1916, xvii, 525.

12. Van Slyke, Cullen and Stillman. Changes in Blood Alkalinity during Digestion, Proc. Soc. for Exp. Biol. and Med., 1915, xii, 184; 112 (1044).

13. Sellards. A Clinical Method for Studying Titratable Alkalinity of the Blood and its Application to Acidosis, Johns Hopkins Hosp. Bull., 1914, xxv, 101.

14. Barcroft. The Respiratory Function of the Blood, Cambridge University Press, 1914.

15. Schaffer and Marriott. The Determination of Acetone. Nephelometric Determination of Minute Quantities of Acetone. The Determination of B-oxybutyric Acid in Blood and Tissues, Jour. Biol. Chem., 1913, xvi, 265.

Marriott. The Blood in Acidosis from the Quantitative Stand-point. Jour. Biol. Chem., 1914, xviii, 507.

16. McClendon. New Hydrogen Electrodes and Rapid Methods of Determining Hydrogen Ion Concentrations, Am. Jour. Physiol., 1915, xxxviii, No. 2, 180.

A Direct Reading Potentiometer for Measuring Hydrogen Ion Concentration, ibid., 1915, xxxviii, No. 2, 186.

17. Abel, Rowntree and Turner. On the Removal of Diffusible Substances from the Circulating Blood of Living Animals by Dialysis, Jour. Pharm. and Exp. Therap., January, 1914, vol. v, No. 3.

II. Some Constituents of the Blood, ibid., July, 1914, vol. v, No. 6.

18. Marriott. The Determination of Alveolar CO_2 Tension by a Simple Method, Jour. Am. Med. Assn., lxvi, No. 21, 1594.

19. Hasselbalch and Gammeltoft. Biochem. Ztschr., 1915, lxviii, 233.

20. Howland and Marriott. Acidosis Occurring with Diarrheas, Am. Jour. Dis. Child, No. 5, xi, 309.

21. Sellards. Tolerance for Alkalies in Asiatic Cholera, Philippine Jour. Sc., 1910, v, 363.

Sellards and Shaklee. Indications of Acid Intoxication in Asiatic Cholera, ibid., 1911, vi, 53.

22. Hasselbalch and Gammeltoft. Die Neutralitätsregulation des graviden Organismus, Biochem. Ztschr., 1915, lxviii, 208. Abstracted in Jour. Am. Med. Assn., October 2, 1915, lxv, 1190.

23. Ehrmann and Esser. Ueber experimentalles Koma, Ztschr. f. klin. Med., 1911, lxxii, 496.

24. Peabody. Am. Jour. Med. Sc., 1916, cli, 184.

25. Hasselbalch and Gammeltoft. Loc. cit.

26. Wilson and Stearns. The Effect of Acid Administration on Parathyroid Tetany, Jour. Biol. Chem., 1915, xxi, 169.